A Mixed-Effects ANOVA Study of Cognition Scores Across Two Visits in Older Adults

1. Introduction

Understanding the indicators for Alzheimer would be crucial as it help doctors to discover it. This study conducts a quantitative analysis of a longitudinal dataset, applying mixed-effects ANOVA to explore the influence of different diagnosis groups and their interaction with two assessments on different cognition scores. Utilizing the dataset 'INF2178_A4_data.csv', we explore how different groups of people show a change in different scores in two successive MRI tests. We will also look at a power analysis at the end to choose the optimal sample size for the particular setting of parameters. Based on these thoughts, we would like to mainly discuss two questions here:

1. **Research Question 1:** How does the progression of nWBV differ among individuals with different cognitive statuses over two visits?
2. **Research Question 2:** How does cognitive scores, as measured by MMSE, change over time in individuals, and does this change differ by cognitive status group?

2. Data Cleaning and Data Wrangling

Our dataset comprised a total of **15 columns** with **294** entities (**rows**), and there is one missing value in column 'MMSE', since this is one of the scores we would like to study, I will drop this null value from the dataset. We will also focus on related columns and leave out other unrelated columns. Below is the description of each related column we would study here:

- **Subject ID:** Unique subject identification for each participant.
- **Group:** Represent different diagnostic categories: "Nondemented," "Converted," and "Demented."
- **Visit:** The specific time points when a participant came in for an assessment: "1" or "2".
- **MMSE:** Mini Mental State Examination
- **nWBV**: Normalize Whole Brain Volume

Since we want to study the within-subject design and repeated measures on the same subjects, which needs comparison of the same subjects across different time points (Visit 1 and Visit 2), I decide to keep only subjects who have completed both visits. After doing that, I have a total of 143 unique subjects and 286 rows of data.

3. Exploratory Data Analysis (EDA)

we will first examine the summary statistics for key variables of interest—specifically, the MMSE and nWBV scores to provide an initial understanding of the data. Then we show boxplots to visually explore the relationships between diagnostic groups, visits and the respective scores for MMSE and nWBV separately to identify any apparent differences in cognitive function and brain volume across groups.

	MMSE	nWBV
count	286	286
mean	27.22	0.73
std	3.44	0.04
min	15	0.65
25%	26	0.70
50%	29	0.73
75%	30	0.76
max	30	0.84

Figure 1: Data Summary Statistic

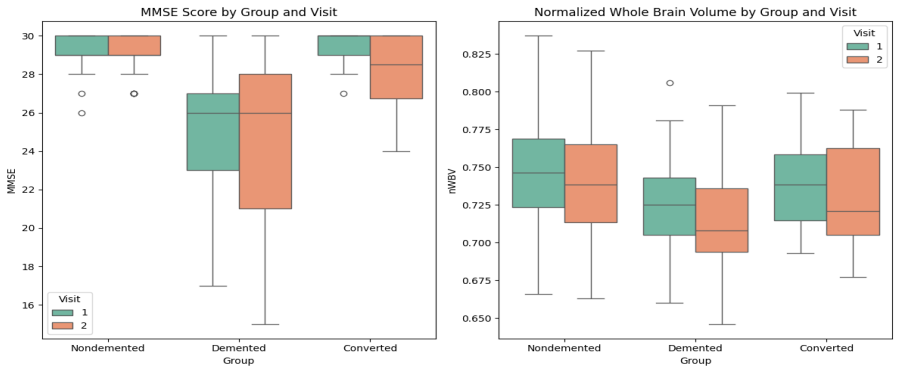

Figure 2: Boxplot of MMSE and nWBV Scores by Group and Visit

Figure 2 shows that for MMSE scores, the nondemented group has higher median scores in both visits, suggesting better cognitive function relative to the other groups. The converted group shows a notable decrease in MMSE scores from Visit 1 to Visit 2, indicating a possible decline in cognitive function over time. In contrast, nWBV scores are more consistent across visits for all groups, but the nondemented group exhibits higher median values, potentially reflecting healthier brain volume. The Demented and Converted groups have similar nWBV distributions in both visits, which may suggest a more advanced or progressing neurological condition. Overall, these visualizations indicate that cognitive function and brain volume vary by diagnostic group and that there may be a cognitive decline over time, especially in the converted group.

4. Examining the Progression of nWBV in Relation to Cognitive Status Over Time

Research Question #1: How does the progression of nWBV differ among individuals with different cognitive statuses over two visits?

In order to address this question, we first look at the interaction plot comparing the mean nWBV for three different groups across two visits. From figure 3 we can see a longitudinal decline in nWBV across all cognitive groups, with the most pronounced decrease observed in the converted group from visit 1 to visit 2, suggesting a diverse progression of brain volume reduction as cognitive status deteriorates. Next, we will apply the mixed-design ANOVA test to see these changes more clearly.

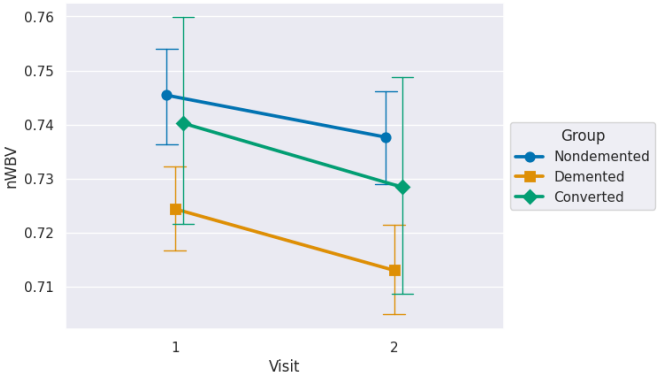

Figure 3: Interaction Plot of nWBV Across Cognitive Groups and Visits

Source	SS	DF1	DF2	F	PR(>F)	η^2
Group	0.034	2	140	6.8	0.002	0.089
Visit	0.007	1	140	97.5	<0.001	0.411
Interaction	0.000	2	140	1.8	0.171	0.025

Figure 4: Mixed-design ANOVA test for nWBV Variability Across Cognitive Statuses and Visits

The null hypothesis is that there are no significant differences in nWBV between different groups, across the two visits, or in the interaction between group and visit time points. Figure 4 suggests significant effects for both 'Group' and 'Visit' on the dependent variable, with p-values below 0.05. However, the interaction between 'Group' and 'Visit' is not statistically significant (p = 0.171), suggesting that the change in brain volume over time does not differ significantly across the groups.

The post-hoc test results reveal a statistically significant decline in nWBV from Visit 1 to Visit 2, indicating a change over time. While the comparisons between the converted group and both the demented and nondemented groups are not significant, there is a notable difference between the demented and nondemented groups, particularly at the second visit where a significant interaction effect is observed.

Shapiro-Wilk			
Visit	**Statistic**	**P-value**	**Normal**
1	0.99	0.37	True
2	0.99	0.34	True

Figure 5: Shapiro-Wilk Test of Normality for Different Visits

Levene's Test		
Statistic	**P-Value**	**Equal Variance**
0.36	0.55	True

Figure 6: Levene's Test for Homogeneity of Variances for Different Visit

In order to properly complete the test, we also need to check if **assumptions** are satisfied. To begin with, the **normality check** was done by the **Shapiro-Wilk test**, and we can see from figure 5 that the normal distribution assumption is satisfied.

Then we conduct **Levene's test** to check the homogeneity of variances for different visits are satisfied. From the test result table on the left, we can see that the assumption of equal variances is also satisfied. We also have the **Mauchly's test of sphericity** and the result (1.0) shows that this assumption is not violated.

5. Examining the Progression of MMSE in Relation to Cognitive Status Over Time

Research Question #2: How does cognitive scores, as measured by MMSE, change over time in individuals, and does this change differ by cognitive status group?

Apart from brain volume, we also want to study how different groups and visits affect MMSE scores, and just like for nWBV, analyzing MMSE scores can provide valuable insights into how cognitive functions change over time and whether these changes differ among various groups of cognitive status, potentially aiding in early detection and intervention strategies for cognitive impairment and dementia.

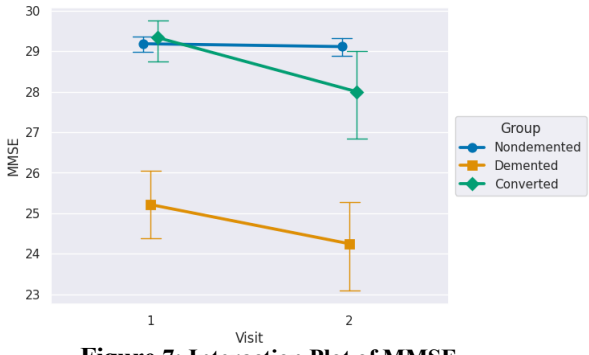

Figure 7: Interaction Plot of MMSE Across Cognitive Groups and Visits

We will first look at the Interception Plot which displays the relationship of MMSE scores between different groups and visits. From figure 7 we can see that nondemented group starting with the highest scores and experiencing a barely decline, while the demented and converted groups start with lower scores and show a more noticeable decrease by Visit 2.

To investigate the research question further, we use another **mixed-design ANOVA** test to see if there are interaction effect between these two features. From the **ANOVA table below**, we can see that there are statistically significant differences in MMSE scores between the groups. The 'Visit' factor also shows significance, suggesting that MMSE scores differ from Visit 1 to Visit 2. The interaction between 'Group' and 'Visit' is statistically significant, indicating that the effect of the visit on MMSE scores differs statistically across the groups.

Source	SS	DF1	DF2	F	PR(>F)	η^2
Group	1328.42	2	140	56.21	<0.001	0.045
Visit	22.38	1	140	8.86	0.003	0.060
Interaction	17	2	140	3.37	0.037	0.046

Figure 8: Mixed-design ANOVA test for MMSE Variability Across Cognitive Statuses and Visits

The post-hoc test here reveals significant differences in MMSE scores across visits and between cognitive groups, with the most pronounced changes occurring between the Demented and Nondemented groups. The interaction of visit and group is significant for the Demented and Nondemented groups, indicating that the progression of cognitive decline as measured by MMSE scores varies significantly between these groups over time.

Just like for the first research question, we should perform **assumption check** to ensure the validity of the test's results for the second research question, and below are the results tables of the normality and homoscedasticity check. It can be seen from the two tables below that the dataset failed normality assumption, but it satisfies the equal variance assumption. We also check the sphericity assumption, and the result (1.0) is satisfied as well.

Shapiro-Wilk			
Visit	Statistic	P-value	Normal
1	0.79	<0.001	False
2	0.76	<0.001	False

Figure 9: Shapiro-Wilk Test of Normality for Different Visits

Levene's Test		
Statistic	P-Value	Equal Variance
1.73	0.19	True

Figure 10: Levene's Test for Homogeneity of Variances for Difference Visits

6. Power Analysis

Finally, we want to perform a power analysis to see the target sample size. Given that we want a power level of 0.91, alpha level of 0.05 and effect size of 0.7, we can calculate it in python and the result is rounded to **46**(**45.45**), and figure 11 is the power plots for our test.

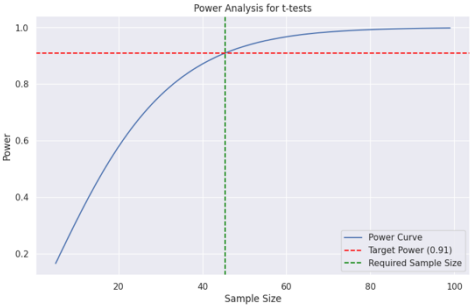

Figure 11: Power Analysis

7. Conclusion

To summarize, this study investigates cognitive changes in older adults through a mixed-effects ANOVA, examining cognition scores across two MRI visits. Initial exploratory analysis reveals differences in cognitive scores across groups and different visits. A significant interaction between group and visit time points was observed for MMSE scores, indicating varying rates of cognitive decline. The study also performs a power analysis, suggesting an optimal sample size for future research. The findings underscore the complexity of cognitive changes in aging, emphasizing the need for targeted interventions based on cognitive status and progression.